

REMARKS

Claims 1-35 were previously cancelled. Claims 36 is amended. Claims 36-41 are pending. The amendment of the existing claims does not affect inventorship. Support for the amendments is found in the specification as filed, see, e.g., Examples 1 and 2.

Claim Rejections – 35 USC § 112, second paragraph

Claims 36-41 are rejected under 35 USC § 112, second paragraph as being unclear. Specifically, "claim 36, it is not clear how applying force field calculation to particular residue, per step c) will result in a library, rather than a set of energy-optimized residues." (Emphasis in Office Action.) Claim 36 has been amended to clarify the force field calculation applies to the plurality of variable positions and the coordinates of the target protein, for example, the entire structure, in order to generate a primary library of variant protein sequences.

The Office Action additionally states, "Further, it is not clear in which way primary library is different from secondary libraries." While every possible variable amino acid at each of the variable residue positions in the secondary library is found in the primary library, the overall sequence of at least one member of the secondary library is not found in the primary library. As discussed below, the way in which the secondary library differs from the primary library is something not taught or suggested by Wang et al (Protein Engineering, 9 (6), 479-484, 1996) or Dahiyat, 1997 (J. Mol. Biol., 1997, 273, 789-796). By way of example, assume a primary library consists of the following sequences:

xExxTxVx

xDxxSxAx

xExxTxLx

xExxSxIx

The resulting secondary library might contain the following sequences:

xExxTxAx

xDxxSxVx

xDxxTxAx

xDxxTxIx

xExxSxIx

In the example above, even though every variable amino acid at each of the variable residue positions in the secondary library is individually found in the primary library, only one of the five sequences in the secondary library is found in the primary library. Thus, the sequences in the secondary library will often be different than sequences in the primary library, and claim 36 requires that at least one sequence in the secondary library is different than any sequence in the primary library.

Applicants believe that claim 36, as amended, is clear and meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants respectfully request this rejection be withdrawn.

Claim Rejections – 35 USC §§ 102 and 103

The rejection of Claims 36-41 are rejected under 35 USC §§ 102 and 103 as being anticipated and made obvious taught or suggested by Wang et al (Protein Engineering, 9 (6), 479-484, 1996) and Dahiyat, 1997 (J. Mol. Biol., 1997, 273, 789-796).

As amended, all pending claims require the generation of a secondary library by using several specific steps. The secondary library is generated by combining an amino acid residue in the set of amino acid residues at each of the variable residue positions. The set of amino acid residues at each of the variable residue positions is generated by both selecting at least one variable amino acid at the relevant variable position from variant protein sequences in the primary library and selecting the amino acid residue of the target protein for the relevant variable position. As amended for clarity, at least one member of the secondary library has a plurality of variant amino acids relative to the target protein.

In relation to Wang, the Office Action states that the "primary library" is the target protein with every amino acid substituted one at a time at every residue. Assuming for argument sake only that this is a primary library, Applicants note that Wang does not teach or suggest the generation of a secondary library by any means, and does not teach or suggest the generation of a sequence not found within the definition of the primary library as given by the Office Action. Further, Wang does not teach or suggest the generation of a secondary library wherein at least one member of the secondary library has a plurality of variant amino acids relative to the target protein. Neither does Dahiyat 1997 teach or suggest these limitations. In relation to Figure 1 of Wang, this is an analysis of the energies of each of the 20 types of amino acids and is not using a force field calculation to generate a secondary library of protein variants. Applicants respectfully submit that Figure 1 of Wang does not teach or suggest steps D) and E) as required in amended claim 36.

Since Wang and Dahiyat 1997 not teach or suggest every limitation found in the amended claims, Applicants respectfully submit that these references cannot anticipate the amended claims. Additionally, no other reference of record teaches or suggests this missing limitation and thus do not make the pending claims obvious. Applicants respectfully request that the rejections under 35 U.S.C. §§ 102 and 103 be withdrawn.

Conclusion

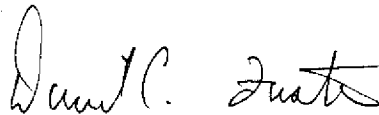
The Applicants submit that in light of the above-amendment and argument, the claims are now in condition for allowance and an early notification of such is respectfully solicited.

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